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Notebook #: 39040  
CAI

EXHIBIT A

## Measurement of SCH 58235 effects on Cholesterol absorption in ApoE KO and Normal Mice

Male ApoE knockout mice, age 6wks, were received from Jackson Laboratory along with age-matched C57BL/6 on 2-18-98. The mice were housed 5/cage, normal light cycle, normal diet.

On 3-6-98, 26 mice of each variety were weighed and housed 1/cage in suspended wire cages in rm GB-78 with normal light cycle, normal diet.

On 3-9-98 the mice were reweighed. Based on BW, the mice were divided into 5 groups for each type: Vehicle, SCH 58235 at 0.3, 1, 3, and 10 mg/kg per day.

Preparation of SCH 58235 soln based on 22g avg BW:

10mg/kg/day in 0.1ml corn oil:  $2.2\text{mg/ml} \times 10\text{ml} = 22\text{mg}$  in 10ml corn oil

3mg/kg: 3 ml of 10mg/kg soln + 7 ml corn oil

1mg/kg: 3 ml of 3mg/kg soln + 6 ml corn oil

0.3mg/kg: 2 ml of 1mg/kg soln + 4.67 ml corn oil

The mice were gavaged using a 24ga feeding needle 30 min before receiving  $^{14}\text{C}$ -cholesterol (NEN, NEC 018) and  $^3\text{H}$ -sitosterol (NEN, CUS 030T). The radioactive soln was prepared:

114  $\mu\text{L}$   $^3\text{H}$ -sitosterol stock (1  $\mu\text{Ci}/\mu\text{L}$  in EtOH)

1.425mL  $^{14}\text{C}$ -cholesterol stock (40  $\mu\text{Ci}/\text{mL}$  in EtOH)

5.7 mg cholesterol, Sigma C 8667

5.7 mg  $\beta$ -sitosterol, Sigma S 1270

The soln was blown dry under  $\text{N}_2$

5.7ml of corn oil was added, warmed to  $60^\circ\text{C}$ ; shaken for 1hr

Each 0.1ml dose contained:  $1\mu\text{Ci}$   $^3\text{H}$ -sitosterol, 0.1mg cold sitosterol;  $1\mu\text{Ci}$   $^{14}\text{C}$ -cholesterol, and 0.1mg cold cholesterol. Radioactive content was verified: 5 X 10  $\mu\text{L}$  counted in Beckman LSC.

On 3-10, 3-11, and 3-12 feces were collected and stored at  $-20^\circ$  in LSC vials just before dosing with vehicle or SCH 58235 late in the day.

Termination of the experiment on 3-13 involved BW detn, fecal collection followed by  $\text{CO}_2$  inactivation, cardiac puncture blood sample, sacrifice by exsanguination, removal and weight of the liver. 3 X ~250mg pieces of liver were put in LSC vials. The liver samples were digested with 1ml of 1N NaOH at  $60^\circ$  overnight, neutralized with 0.1ml 12N HCl and counted. The blood samples were allowed to clot at room temp for 1hr, then centrifuged at 1000G for 15 min. The serum was analyzed for total cholesterol (Wako CII) and radioactivity (2 X 50  $\mu\text{L}$ ). Fecal samples were analyzed for radioactivity by combustion in a Packard Oxidizer.

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Sheet1

Mice transferred to wire cages & individually housed for acclimation: 3/6/98							
Body weights taken again on 3/9/98, mice grouped according to these BW							
SORT By Body Wt.							
C57/BLJ	BW(3-9)	Rank	Grp Mean	ApoE-KO	BW(3-9)	Rank	Grp Mean
10 8	24	5		4	23	5	
2	23.4	5		7 DEAD 3/10	22.7	5	
11	21.2	5		12	21.4	5	
17	20.3	5		(16)	17.2	5	
(18)	16.1	5	21.0	3	22.4	5	21.3
3 15	24.4	4		9	24.6	4	
5	23.4	4		8	22.7	4	
22	21.6	4		15	22	4	
20	20.7	4		13	21.5	4	
(12)	17.1	4	21.4	21	19.1	4	22.0
1 19	24.5	3		1	24.9	3	
3	23.2	3		19	22.5	3	
23	22	3		(26)	22.2	3	found dead 3-11
(7)	20.8	3		10	21.7	3	
(6)	17.6	3	21.6	17	20.7	3	22.4
4	24.9	2		11	21.8	2	
16	23.1	2		5	25.3	2	
0.3 21	20.9	2		22	21.8	2	
(14)	18.8	2		24	21.2	2	
10	20.1	2	21.6	14	21.8	2	22.4
24	21.2	1		22	22.2	1	
1	25.8	1		6	25.4	1	
0 13	23	1		20	22.4	1	
9	22.9	1		18	22.3	1	
25	22.5	1		25	21.3	1	
(26)	14.4	1	21.7	(2)	16.8	1	21.8

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C57/BLJ & ApoE-KO Mouse									
Dual label CAL (3H-cholesterol, 14C-cholesterol)									
C57/BLJ					ApoE-KO				
#	BW3-6	BW3-9	BW3-13	A	#	BW3-6	BW3-9	BW3-13	A
8	25	24	25	1.0	4	23.5	23	23.5	0.5
2	21.2	23.4	22.9	-0.6	7	22.7	22.7		
11	22.9	21.2	22.3	1.1	3	22.1	22.4	22.3	-0.1
17	20.4	20.3	20.6	0.3	13	21.6	21.4	22.3	0.9
18	19.2	16.1	20	3.9	16	22	17.2	22.4	5.2
SCH 58235, 10mg/kg/day									
	21.7	21.0	22.1	1.1		22.4	21.3	22.6	1.6
	±1.0	±1.4	±0.9	±0.8		±0.3	±1.1	±0.3	±1.2
15	22.8	24.4	24	-0.4	9	25	24.6	25	0.4
5	22.2	23.4	23.8	0.5	8	23.2	22.7	23.5	0.8
22	22.2	21.6	17	-4.5	15	22.3	22	22.2	0.2
20	21.3	20.7	20	-0.7	12	21.7	21.5	21.6	0.1
12	21.7	17.1	23	5.9	21	18.5	19.1	18.5	0.4
SCH 58235, 3mg/kg/day									
	22.9	21.4	21.8	0.1		22.4	22.0	22.4	0.4
	±0.3	±1.3	±1.4	±1.7		±0.8	±0.9	±0.9	±0.1
19	24.8	24.5	25	0.5	1	24.6	24.9	23.8	-1.1
3	24.2	23.2	17.3	-5.9	18	21.5	22.5	21.8	-0.7
23	22.5	22	22.2	0.2	26	22.7	22.2		
7	23	20.8	19.6	-1.9	10	22.4	21.7	22.3	0.8
6	22.1	17.8	22.3	4.7	17	22	20.7	20.9	0.2
SCH 58235, 1mg/kg/day									
	23.6	21.8	21.3	-0.3		22.6	22.4	22.2	-0.2
	±0.6	±1.2	±1.3	±1.7		±0.5	±0.7	±0.6	±0.4
4	26.3	24.8	24.6	-0.3	5	25.2	25.3	24.8	-0.5
16	21.6	20.1	22.7	-0.4	11	21.5	21.8	19.4	-2.4
21	21.1	20.8	21.3	0.4	14	22	21.8	21.7	-0.1
18	21.1	20.1	20.5	0.5	22	22.3	21.8	22	0.2
14	24.8	18.8	23.6	4.8	24	21.4	21.2	20.3	-0.9
SCH 58235, 0.3mg/kg/day									
	23.0	21.6	22.5	1.0		22.7	22.4	21.6	-0.7
	±1.1	±1.1	±0.7	±1.0		±0.9	±0.7	±0.8	±0.5
1	24.5	25.8	19.3	-5.6	5	24.9	25.4	25.1	-0.3
19	18.7	23	23.3	0.3	20	22	22.4	21.5	-0.8
8	24.2	22.9	23.4	0.5	18	22.5	22.3	22.5	0.2
25	18.8	22.5	23.1	0.6	23	22.5	22.2	22.2	0.8
26	21.5	21.3	21.7	0.5	25	21.8	21.8	22	0.7
28	17.5	14.4	19.7	5.3	2	22.1	16.8	22.3	5.5
Vehicle, 0.1ml corn oil/day									
MEAN	20.9	21.8	21.6	0.1		22.5	21.7	22.5	0.9
	±1.2	±1.6	±0.8	±1.5		±0.5	±1.1	±0.8	±0.9

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CAI 3-9-98		MOUSE STUDY		EROL/CHOLESTEROL CHRONIC DOSING		
C57BL/6J		Sex		Total DPM		Serum
#	treatment	H-DPM	C-DPM	H-DPM	C-DPM	Cholesterol mg/dl
8	SCH 58235-10mg/kg			3589	3670	
2	SCH 58235-10mg/kg	192	30	1774	3079	85
11	SCH 58235-10mg/kg	25	62	2703	3551	87
17	SCH 58235-10mg/kg	201	148	6626	5992	85
18	SCH 58235-10mg/kg	90	72	1770	7013	79
15	SCH 58235-3mg/kg	92	149	1770	11456	83
5	SCH 58235-3mg/kg	52	193	3629	11359	73
22	SCH 58235-3mg/kg	126	67	30944	17258	76
20	SCH 58235-3mg/kg	8	138	3068	10111	76
12	SCH 58235-3mg/kg	499	114	3203	11335	97
19	SCH 58235-1mg/kg	87	212	3844	13972	92
3	SCH 58235-1mg/kg	79	253	2246	16032	82
23	SCH 58235-1mg/kg	153	165	1787	13805	70
7	SCH 58235-1mg/kg	143	162	5620	12779	83
6	SCH 58235-1mg/kg	211	279	4037	21194	94
4	SCH 58235-0.3mg/kg	102	1142	7280	45822	85
16	SCH 58235-0.3mg/kg	48	632	8437	32834	94
21	SCH 58235-0.3mg/kg	10	838	7550	53592	92
14	SCH 58235-0.3mg/kg	11	772	3582	46037	105
10	SCH 58235-0.3mg/kg	68	435	5794	22108	94
24	Vehicle, 0.1ml corn oil	43	1329	6202	81714	92
1	Vehicle, 0.1ml corn oil	627	832	11267	34738	128
13	Vehicle, 0.1ml corn oil	127	1249	5330	88089	98
9	Vehicle, 0.1ml corn oil	143	1423	2226	103754	88
25	Vehicle, 0.1ml corn oil	63	1518	14109	59724	100
26	Vehicle, 0.1ml corn oil	110	1842	13756	53361	122
ApoEKO						
4	SCH 58235-10mg/kg	803	713	7681	7491	546
12	SCH 58235-10mg/kg	127	298	2905	4377	829
15	SCH 58235-10mg/kg	65	367	3485	5483	579
3	SCH 58235-10mg/kg	89	1268	4530	14566	402
9	SCH 58235-3mg/kg	236	1235	5481	8088	587
8	SCH 58235-3mg/kg	288	631	4866	7796	409
15	SCH 58235-3mg/kg	146	986	4790	9613	481
13	SCH 58235-3mg/kg	301	961	4072	9943	443
21	SCH 58235-3mg/kg	335	1022	3794	7481	710
1	SCH 58235-1mg/kg	0	2368	9852	23280	405
18	SCH 58235-1mg/kg	0	2189	6309	31695	386
10	SCH 58235-1mg/kg	137	2710	4986	15097	847
17	SCH 58235-1mg/kg	57	1632	3341	21018	492
11	SCH 58235-0.3mg/kg	12	3621	11193	51090	416
5	SCH 58235-0.3mg/kg	446	7598	16426	52660	871
22	SCH 58235-0.3mg/kg	182	6640	10725	86583	718
24	SCH 58235-0.3mg/kg	269	5458	8579	40888	669
14	SCH 58235-0.3mg/kg	66	7868	7619	64917	705
8	Vehicle, 0.1ml corn oil	381	10133	15085	92537	663
20	Vehicle, 0.1ml corn oil	580	13554	35081	82942	753
23	Vehicle, 0.1ml corn oil	151	7552	28479	82301	523
18	Vehicle, 0.1ml corn oil	234	12690	18231	121537	616
25	Vehicle, 0.1ml corn oil	358	11760	17897	97945	772
2	Vehicle, 0.1ml corn oil	343	7741	19678	89964	735

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CAI 3-9-98		MOUSE STEROL/CHOLESTEROL CHRONIC DOSING			
C57/BLJ		Serum		Liver	
# treatment	<sup>3</sup> H-DPM	<sup>14</sup> C-DPM	<sup>3</sup> H-DPM	<sup>14</sup> C-DPM	Cholesterol mg/dL
Vehicle, 0.1ml corn oil					
mean	186	1332	8815	70230	104
sem	±90	±115	±2007	±10375	±7
SCH 58235-0.3mg/kg					
mean	48	764	6513	40079	94
sem	±17	±117	±853	±5597	±3
SCH 58235-1mg/kg					
mean	134	214	3507	15556	84
sem	±24	±23	±686	±1505	±4
SCH 58235-3mg/kg					
mean	156	132	2818	11065	81
sem	±88	±21	±401	±319	±4
without liver values from mouse #22					
SCH 58235-10mg/kg					
mean	127	78	3292	4661	84
sem	±42	±25	±699	±775	±2
ApoE KO					
Vehicle, 0.1ml corn oil					
mean	338	10572	22492	94536	677
sem	±59	±1035	±3129	±5815	±39
SCH 58235-0.3mg/kg					
mean	195	6237	11106	53230	676
sem	±77	±778	±1485	±8906	±74
SCH 58235-1mg/kg					
mean	49	2225	6072	22779	533
sem	±32	±225	±1339	±3438	±107
SCH 58235-3mg/kg					
mean	261	967	4610	8584	528
sem	±33	±97	±301	±499	±54
SCH 58235-10mg/kg					
mean	271	662	4650	7979	464
sem	±178	±222	±1065	±2288	±59

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CAI 3-9-98		MOUSE SITOSTEROL/CHOLESTEROL CHRONIC DOSING			
CS7BL/J		% of Administered Dose			
		Serum		Liver	
#	Treatment	<sup>3</sup> H-DPM	<sup>14</sup> C-DPM	<sup>3</sup> H-DPM	<sup>14</sup> C-DPM
8	SCH 58235 10mg/kg			0.060	0.136
2	SCH 58235 10mg/kg	0.003	0.001	0.030	0.114
11	SCH 58235 10mg/kg	0.000	0.002	0.045	0.132
17	SCH 58235 10mg/kg	0.003	0.005	0.111	0.222
18	SCH 58235 10mg/kg	0.002	0.003	0.030	0.260
15	SCH 58235 1mg/kg	0.002	0.006	0.030	0.425
5	SCH 58235 1mg/kg	0.001	0.007	0.081	0.421
22	SCH 58235 1mg/kg	0.002	0.002	0.519	0.640
20	SCH 58235 1mg/kg	0.000	0.005	0.051	0.375
12	SCH 58235 1mg/kg	0.008	0.004	0.054	0.420
19	SCH 58235 1mg/kg	0.001	0.008	0.054	0.518
3	SCH 58235 1mg/kg	0.001	0.009	0.038	0.594
23	SCH 58235 1mg/kg	0.003	0.006	0.030	0.512
7	SCH 58235 1mg/kg	0.002	0.008	0.094	0.474
6	SCH 58235 1mg/kg	0.004	0.010	0.058	0.788
4	SCH 58235 1.3mg/kg	0.002	0.042	0.122	1.699
16	SCH 58235 1.3mg/kg	0.001	0.023	0.142	1.217
21	SCH 58235 1.3mg/kg	0.000	0.031	0.127	1.967
14	SCH 58235 1.3mg/kg	0.000	0.029	0.030	1.707
10	SCH 58235 1.3mg/kg	0.001	0.016	0.096	0.820
24	Vehicle, 0.1ml corn oil	0.001	0.048	0.104	3.030
1	Vehicle, 0.1ml corn oil	0.011	0.031	0.189	1.288
13	Vehicle, 0.1ml corn oil	0.002	0.046	0.089	3.266
9	Vehicle, 0.1ml corn oil	0.002	0.053	0.037	3.847
25	Vehicle, 0.1ml corn oil	0.001	0.055	0.237	2.214
26	Vehicle, 0.1ml corn oil	0.002	0.061	0.231	1.978
AppE KO					
4	SCH 58235 0mg/kg	0.013	0.026	0.129	0.278
12	SCH 58235 0mg/kg	0.002	0.011	0.049	0.162
16	SCH 58235 0mg/kg	0.001	0.014	0.058	0.203
3	SCH 58235 0mg/kg	0.001	0.047	0.076	0.540
8	SCH 58235 1mg/kg	0.004	0.048	0.082	0.300
8	SCH 58235 1mg/kg	0.005	0.023	0.082	0.288
15	SCH 58235 1mg/kg	0.002	0.037	0.060	0.356
13	SCH 58235 1mg/kg	0.005	0.036	0.068	0.368
21	SCH 58235 1mg/kg	0.006	0.038	0.064	0.277
1	SCH 58235 1mg/kg	0.000	0.088	0.152	0.883
18	SCH 58235 1mg/kg	0.000	0.081	0.106	1.176
10	SCH 58235 1mg/kg	0.002	0.100	0.084	0.560
17	SCH 58235 1mg/kg	0.001	0.061	0.056	0.779
11	SCH 58235 1.3mg/kg	0.000	0.134	0.188	1.894
5	SCH 58235 1.3mg/kg	0.007	0.282	0.276	1.952
22	SCH 58235 1.3mg/kg	0.003	0.246	0.180	2.098
24	SCH 58235 1.3mg/kg	0.005	0.202	0.161	1.516
14	SCH 58235 1.3mg/kg	0.001	0.292	0.128	2.407
6	Vehicle, 0.1ml corn oil	0.006	0.378	0.253	3.431
20	Vehicle, 0.1ml corn oil	0.010	0.503	0.588	3.075
23	Vehicle, 0.1ml corn oil	0.003	0.280	0.478	3.051
19	Vehicle, 0.1ml corn oil	0.004	0.470	0.323	4.506
25	Vehicle, 0.1ml corn oil	0.006	0.436	0.292	3.631
2	Vehicle, 0.1ml corn oil	0.006	0.287	0.330	3.395

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CAI 3-9-98		MOUSE S1 OSTEROL/CHOLESTEROL CHRONIC DOSING			
C57BL/6J		% of Radioactivity administered			
treatment		<sup>3</sup> H	<sup>14</sup> C	<sup>3</sup> H	<sup>14</sup> C
Vehicle, 0.1ml corn oil					
	mean	0.003	0.05	0.15	2.60
	sem	±0.002	±0.00	±0.03	±0.38
SCH 58235-0.3mg/kg					
	mean	0.001	0.03	0.11	1.49
	sem	±0.000	±0.00	±0.01	±0.21
SCH 58235-1mg/kg					
	mean	0.002	0.01	0.05	0.58
	sem	±0.000	±0.00	±0.01	±0.06
SCH 58235-3mg/kg					
	mean	0.003	0.005	0.14	0.46
	sem	±0.001	±0.001	±0.03	±0.05
SCH 58235-10mg/kg					
	mean	0.002	0.003	0.06	0.17
	sem	±0.001	±0.001	±0.02	±0.03
ApoE KO					
Vehicle, 0.1ml corn oil					
	mean	0.006	0.395	0.40	3.52
	sem	±0.001	±0.047	±0.06	±0.27
SCH 58235-0.3mg/kg					
	mean	0.003	0.231	0.13	1.97
	sem	±0.001	±0.023	±0.02	±0.14
SCH 58235-1mg/kg					
	mean	0.001	0.082	0.10	0.84
	sem	±0.001	±0.003	±0.02	±0.13
SCH 58235-3mg/kg					
	mean	0.004	0.036	0.06	0.32
	sem	±0.001	±0.004	±0.01	±0.02
SCH 58235-10mg/kg					
	mean	0.005	0.025	0.08	0.30
	sem	±0.003	±0.003	±0.02	±0.08

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CAI 3-9-98		MOUSE		STEROID/CHOLESTEROL CHRONIC DOSING				FECES	
				% Radioactivity administered					
DAY 1				DAY 1					
C57BL/J				<sup>14</sup> C-dpm		<sup>14</sup> C		<sup>3</sup> H-dpm	
#	a	b		dpm	%	a	b	dpm	%
8	887125			887033	32.8	2025421		2025331	34.0
8	975421	88:718		1861047	69.0	2258000	1886947	4244857	71.2
11	783937	102:322		1810768	67.1	1854147	2928770	4182827	70.2
17	358181			358068	13.3	889851		889861	14.9
18	982898			982803	38.8	2313066		2312976	38.8
19	2128261			2128184	78.9	5370708		5370618	80.1
5	1641868			1641775	60.9	4087620		4087530	68.6
23	23053			22860	0.9	23663		23573	0.4
28	1082450	98:328		2048386	76.0	2598855	2248145	4845910	81.3
12	1718945			1718852	63.7	4545208		4545118	76.2
13	1786223			1786188	65.5	4782818		4782728	80.2
3	1854941			1854848	68.6	4755250		4755160	79.8
23	1419594			1419501	62.6	3891168		3891078	81.9
7	92109			92016	3.4	266301		266211	4.5
6	1883467			1883364	70.2	4410592		4410502	74.0
4	1357888			1357878	50.3	4859352		4859262	81.6
16	1285373			1285280	47.8	4300444		4300354	72.3
21	1501587			1501484	65.7	5427541		5427451	91.0
14	1122234			1122141	41.8	4158850		4158760	68.8
10	1367878			1367788	60.7	4385834		4385744	73.7
24	829534			829441	20.8	4265085		4264995	71.5
1	74080			73987	2.7	344074		343984	5.8
13	621682			621589	23.0	4441072		4440982	74.5
9	542867			542874	20.1	3878758		3878668	81.7
26	776384			776291	28.7	4732873		4732783	79.4
26	620288			620195	30.4	4838792		4838702	81.8
DAY 1				DAY 1					
ApoE KO				<sup>14</sup> C-dpm		<sup>14</sup> C		<sup>3</sup> H-dpm	
#	a	b		dpm	%	a	b	dpm	%
4	68731			66636	2.5	156483		156373	2.6
7	434470			434377	18.1	1045418		1045328	17.5
12	1669636			1669842	81.9	4131861		4131871	69.3
16	1327886			1327903	49.8	2895223		2895133	50.2
3	1447442			1447348	53.7	3648363		3648273	61.2
8	1782195			1782102	63.4	4290282		4290192	72.0
8	2088858			2088766	77.8	4972336		4972246	83.4
16	1028286	742:30		1771333	65.7	2458834	1808870	4268714	71.8
18	1878821			1878728	69.7	4708750		4708660	79.0
21	1869088			1869005	79.0	4820188		4820108	77.5
1	933882	628:16		1583285	68.0	2881014	1740882	4421906	74.2
18	886519	616:16		1601782	59.4	2126043	1702708	4828661	81.0
26	834846			834753	23.6	1815768		1815678	30.6
18	885834	892:18		1847938	68.5	2457416	2115450	4572776	78.7
17	1893828			1893636	73.0	5462382		5462292	81.6
11	1895844			1895851	81.8	4748920		4748830	79.8
6	1432036			1431948	53.1	4766683		4766593	80.0
22	1157308			1157215	42.0	4198282		4198192	70.4
24	1142145			1142052	42.3	3812484		3812394	64.0
14	1354544			1354451	50.2	4908010		4907920	62.3
8	727382			727289	27.0	4246184		4246094	71.2
28	626006	333:0		850062	31.8	2809208	1717769	4520885	75.8
23	648012			648018	24.1	4584285		4584195	76.6
28	548788			548783	20.3	8588716		8588626	80.4
28	483518			483423	17.2	4350620		4350530	76.3
2	1042868	888:0		1108495	41.1	4491404	186393	4588644	75.8

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CAI 3-9-98				MOUSE SITOSTEROL				CHOLESTEROL CHRONIC DOSING					
% of Radioactivity administered													
DAY 2				DAY 2									
C57BL/J													
#	a	b	dpm	%	a	b	dpm	%	a	b	dpm	%	%
8	101453		1013	3.8	110529		110439	1.9					
2	89217		99	7	91423		81403	1.5					
11	129380		128	0	235560		235490	4.0					
17	108957	81813	100	10	188818	144990	334718	5.8					
18	1059949		1059	9	2293715		2293625	38.5					
15	62152	42984	105	16	27081	14193	41184	0.7					
5	116004		115	4	141156		141056	2.4					
22	12112		12	2	14258		14198	0.2					
20	58995		58	15	19256		18166	0.3					
12	183309	83024	266	13	270851	74712	344973	6.8					
19	126290	67248	192	18	183006	24155	157071	2.6					
3	120207		120	7	70983		70863	1.2					
23	174876		174	18	177141		177051	3.0					
7	284632		284	12	742171		742081	12.4					
6	169423		169	13	210650		210560	3.5					
4	140934		140	14	68028		67938	1.1					
16	113118	49310	182	16	32640	12986	45536	0.8					
21	130916		130	15	83968		83878	0.6					
14	195022		195	12	219088		218998	5.4					
10	127161		127	11	33821		33601	0.6					
24	138881		138	11	136069		135808	2.3					
1	37548		37	10	261843		261853	4.4					
13	110282	56870	187	12	37957	20188	58035	1.0					
9	180874		180	14	43688		43608	0.7					
25	202150		202	10	145620		145530	2.4					
26	558832		558	13	861737		861667	16.1					
DAY 2				DAY 2									
APOE KO													
#	a	b	dpm	%	a	b	dpm	%	a	b	dpm	%	%
4	35174		35	14	72811		72721	1.8					
7													
12	250770		250	10	358648		358558	6.0					
16	287324	170950	458	14	569985	328878	898754	15.1					
3	167826		167	18	348614		348784	5.8					
8	177892		177	10	818011		817931	9.3					
8	186630	33337	218	7	382130	8855	371864	6.2					
15	43101	36788	79	17	23830	22288	48129	0.8					
13	131778		131	16	234432		234402	3.8					
21	114420	39864	154	14	185038	29877	214885	3.6					
1	75668		75	8	41038		40919	0.7					
18	62881	44468	107	19	18714	12242	31824	0.5					
26					880635		880664	16.4					
10	71860		71	0	40603		40593	0.7					
17	107272		107	2	40282		40182	0.7					
11	100716		100	6	22419		22359	0.4					
5	119887		119	7	68762		68662	1.2					
22	123838	88236	209	2	165810	69585	174825	2.9					
24	148084		147	4	373012		372812	6.3					
14	60508	55028	115	4	34001	25778	50888	1.0					
6	111293	89292	209	5	128012	82883	210522	3.6					
20	108348	153808	2620	7	225517	20061	426518	7.1					
29	89433	63144	1524	7	108815	28752	139239	2.3					
18	126178		126	8	100235		100146	1.7					
23	154024		154	1	166605		166788	2.8					
2	73269	85188	188	17	98873	130322	230103	3.9					

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B. Takahashi

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C. Williams

DATE

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CAI 3-9-98			TOSTEROL/CHOLESTEROL CHRONIC DOSING							
% of Radioactivity			Intraperitoneal		Intramuscular		Intravenous		Feces	
DAY 3			DAY 3		DAY 3		DAY 3		DAY 3	
C57BL/J			C-dpm		C-dpm		C-dpm		C-dpm	
#	a	b	dpm	%	dpm	%	dpm	%	dpm	%
1	18011		17921	0.7	3405				3315	0.1
2	19336		19246	0.7	3315				3223	0.1
11	25846		26756	1.0	34519				34428	0.8
17	22585	12	34675	1.3	42413		24785		67108	1.1
18	86562		86472	3.2	98613				98523	1.7
19	27399		27309	1.0	4073				3983	0.1
8	54248		54158	2.0	64509				64419	1.1
22	10954		10884	0.4	15214				15124	0.9
20	28838		22745	0.8	3497				8407	0.1
12	30303	1524	182675	8.8	18859		822795		839565	14.1
18	38644		30554	1.1	3736				3646	0.1
9	39240		35160	1.3	7356				7266	0.1
23	124373		124283	4.8	243315				243225	4.1
7	23448		23358	0.9	21687				21497	0.4
6	28208	192	48108	1.8	5198		3583		8672	0.1
4	38444	334	71810	2.7	2848		6918		8377	0.1
16	33938	549	88831	3.9	11272		97786		108978	1.8
21	45847	387	84510	3.1	5060		4228		9199	0.2
14	49427	403	89671	3.8	18550		18498		34968	0.8
10	33950	277	81635	2.3	4910		2781		7811	0.1
24	84132		84042	3.1	49044				48954	0.8
1	16655		16585	0.6	31752				31682	0.5
13	74807	487	121478	4.5	14056		6180		20156	0.3
9	90784		90694	3.4	10922				10832	0.2
25	90878		90788	3.4	16533				16443	0.9
26	118387		116287	4.3	65018				65928	1.1
DAY 3			DAY 3		DAY 3		DAY 3		DAY 3	
ApoE KO			C-dpm		C-dpm		C-dpm		C-dpm	
#	a	b	dpm	%	dpm	%	dpm	%	dpm	%
4	5500	400	8507	0.2	15626		12355		27891	0.5
7										
12	17773	1218	29885	0.5	12107		8453		20470	0.3
16	12884	1309	25864	0.4	11501		12833		24344	0.4
3	15465	1341	29782	0.5	18621		10884		28818	0.5
9	9812	1284	22668	0.4	4695		5404		10008	0.2
8	13843	841	22264	0.4	2204		1876		3689	0.1
15	14105	1003	24051	0.4	3258		8102		6270	0.1
13	14805	1121	26026	0.4	10420		6955		17285	0.3
21	13451	860	22058	0.4	11084		7384		18528	0.3
1	20808	1884	38565	0.7	8072		3147		11129	0.2
18	46088		44818	0.8	10606				18518	0.2
26										
10	12101	883	20844	0.3	2062		1800		3872	0.1
17	33366		38278	0.6	4084				4894	0.1
11	32142	25558	57608	1.0	6922		4451		10193	0.2
6	27272	18301	45483	0.8	8116		8103		16219	0.3
22	26543	24012	80585	1.0	18810		7102		23822	0.4
24	48383		48283	0.8	90344				90254	1.5
14	31118	17402	48431	0.8	7258		3306		10554	0.2
9	34283	22732	86876	1.0	10386		8305		18673	0.3
20	98444		89354	1.7	256801				256711	4.3
23	43889	33381	77160	1.3	15480		8584		24884	0.4
18	37108	19801	58919	1.0	17120		8848		25878	0.4
25	36987	20288	58562	0.9	30621		17364		47836	0.8
2	22958	25366	57624	1.0	26272		10385		35877	0.6

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DATE .....

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MOUSE CAI 3-98 FECAL RADIOACTIVITY									
C57BL/J									
Total % Administered									
#	<sup>14</sup> C-dpm	<sup>3</sup> H-dpm	mean( <sup>14</sup> C )	<sup>3</sup> H-dpm	Absorbed	mean	±sem	Rx	
8	37.3	35.9	58	±11.5	-3.97	-0.54	±1.02	SCH 58235	
2	73.4	72.8	56	±11.7	-0.81			10mg/kg/day	
11	72.9	74.7			2.38				
17	21.6	21.7			0.18				
18	79.3	78.8			-0.47				
15	83.8	80.9	63	±15.4	7.76	8.66	±2.78	SCH 58235	
5	67.2	72.0	59	±17.3	6.73			3mg/kg/day	
22	1.7	0.9							
20	78.9	81.7			3.33				
12	80.4	88.1			16.38				
19	73.8	82.9	61	±11.8	11.09	6.38	±2.51	SCH 58235	
3	74.8	81.1	65	±12.3	7.88			1mg/kg/day	
23	63.7	69.0			7.62				
7	14.8	17.3							
8	78.8	77.7			-0.76				
4	58.2	82.8	57	±1.8	20.67	27.53	±1.82	SCH 58235	
15	57.1	74.9	79	±3.3	23.78			0.3mg/kg/day	
21	83.6	91.8			30.67				
14	52.2	75.7			31.06				
19	57.7	74.4			22.47				
24	39.5	74.7	83	±8.8	47.78	51.15	±1.97	Vehicle	
1	4.7	10.7	87	±12.3	58.62			1ml corn oil/day	
13	33.7	75.8			55.49				
9	29.4	62.8			52.96				
25	38.6	82.1			51.77				
26	55.8	98.4			43.29				
ApoE KO									
Total % Administered									
#	<sup>14</sup> C-dpm	<sup>3</sup> H-dpm	mean( <sup>14</sup> C )	<sup>3</sup> H-dpm	Absorbed	mean	±sem	Rx	
4	8.9	4.3	50	±15.7		4.79	±3.45	SCH 58235	
7			53	±16.5				10mg/kg/day	
12	71.7	76.7			5.26				
16	66.7	65.7			-1.40				
3	80.4	87.5			10.51				
9	72.3	77.5	78	±3.0	6.82	5.58	±1.24	SCH 58235	
8	85.3	89.7	80	±2.9	3.76			3mg/kg/day	
16	89.0	72.5			4.79				
13	75.0	83.2			9.89				
21	79.1	81.4			2.85				
1	61.5	75.1	88	±3.8	18.01	15.58	±2.95	SCH 58235	
19	84.1	81.7	81	±3.8	21.55			1mg/kg/day	
26									
10	71.5	77.5			7.65				
17	78.4	82.4			15.10				
11	58.4	80.2	54	±1.7	28.60	30.77	±9.97	SCH 58235	
5	58.3	81.4	78	±2.3	28.38			0.3mg/kg/day	
22	51.7	73.8			29.91				
24	48.7	71.7			32.17				
14	65.3	83.6			33.78				
6	35.4	75.1	34	±3.9	52.81	55.52	±4.18	Vehicle	
20	43.2	87.3	77	±3.4	60.47			1ml corn oil/day	
23	31.0	79.2			60.80				
18	29.9	88.6			58.55				
25	23.8	78.9			70.18				
2	48.0	80.1			40.08				

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